REMARKS

The Office Action mailed March 4, 2010 presents the examination of claims 1-3 and 5-11, claims 14 and 16-20 being withdrawn from consideration. The present paper cancels claims 6 and 7, relating to a nucleic acid complex, and also cancels the withdrawn claims 14 and 16-20. New claims 22-24 are added for the Examiner's consideration.

Applicants reserve the right to pursue the subject matter canceled from this application in a further application filed pursuant to 35 USC § 120.

Support for new claims 22-24 is provided in the specification at least at page 14, lines 9-12, and by the working examples 2 and 3 at pages 19 and 20.

Rejections over prior art

Claims 1-3, 5-6 and 8-11 are rejected under 35 USC § 103(a) as being unpatentable over Li '475, Haberland (1999), Haberland (2000) and Lam (2000). This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Applicants submit that the Examiner fails to establish *prima facie* obviousness of the claimed invention, and furthermore, the specification provides results that are not expected by one of ordinary skill in the art who reads the collection of references cited.

All of Li '475, Haberland (1999), Haberland (2000) and Lam (2000) disclose that the nucleic acid being introduced into the cells is complexed with a further substance, and thus these references teach an artisan about "complex-mediated" transformations. Li '475 is directed to transformation of organisms using dsRNA or siRNA. To the degree that transformation of cells maintained in culture is described, Li '475 describes use of "lipid-mediated" transformation, electroporation or "soaking" the cells in a solution of the nucleic acid. Use of calcium phosphate is mentioned in passing and thus the usual manner of adding it to the nucleic acid prior to adding the complex to the cells is plainly intended, and the use of microinjection is said to be preferred. The two Haberland references describe complexes made with cationic lipid, and cationic proteins that are histone proteins, high mobility group proteins or polylysine. In the instance of Lam (2000). the complex is with cationic liposomes (*e.g.*, "Introduction" and section 2.3 "*Lipids and*

chemicals"). Thus, none of these references suggests to the skilled artisan that the nucleic acid should be added to cells without complexation with another substance.

The collection of Li '475, Haberland (1999), Haberland (2000) and Lam (2000) thus fails to establish *prima facie* obviousness of the invention, since the collected references either fail to disclose transforming cells without first complexing the nucleic acid or fail to establish an expectation of success that cells can be transformed by the method of the present invention without first complexing the nucleic acid with some sort of polycationic substance.

Furthermore, at least as to new claims 22-24, none of the references cited by the Examiner describe or suggest that the nucleic acid should be absorbed onto a surface of a cell culturing vessel and then the cells added to the vessel, and then finally a calcium chloride solution added to the cultured cells. Thus, at least these new claims should be found allowable over the references cited.

Furthermore, the present invention can be viewed as providing a result not expected by one of ordinary skill in the art who reads the collection of references. In particular, the Example 4 and results shown in Figure 4 show that delivery of a siRNA to cells is enhanced by application of a high concentration solution of calcium chloride without use of any liposome or other complexation of the siRNA. As disclosed in the Background and Industrial Applicability sections of the specification, this result provides a method that enables transfer of a nucleic acid into cells without the need to process the sample to form a liposome or other complex and providing the associated convenience of use, and the omission of these reagents provides a nucleic acid transfer method that is less cytotoxic than the methods available in the prior art of record.

Claim 7 is rejected under 35 USC § 103(a) as being unpatentable over Li '475, Haberland (1999), Haberland (2000), Lam (2000) and Kubota '840. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Claim 7 is canceled herein, rendering this rejection moot.

Applicants believe the pending application is in condition for allowance, and such favorable action is respectfully requested.

The period for response to the Office Action is extended by three (3) months, to September 4, 2010, by petition filed herewith.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Ph.D., Reg. No. 36,623, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated:. September 7, 2010

Respectfully submitted,

By_____

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